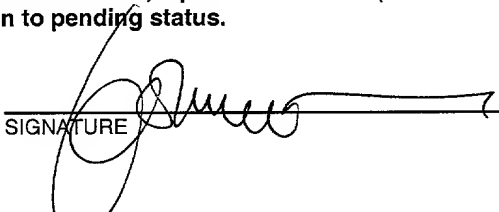


FORM PTO-1390 (REV 11-98)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTORNEY'S DOCKET NUMBER <b>3652-33</b>
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.5) <b>09/786510</b> Unassigned
INTERNATIONAL APPLICATION NO. <b>PCT/NZ00/00063</b>	INTERNATIONAL FILING DATE <b>26 April 2000</b>	PRIORITY DATE CLAIMED <b>21 April 1999</b>
TITLE OF INVENTION <b>METHOD AND SYSTEM FOR MEASURING CHARACTERISTICS OF AN ORGAN</b>		
APPLICANT(S) FOR DO/EO/US <b>COWAN et al</b>		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<p>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19<sup>th</sup> month from the earliest claimed priority date.</p> <p>5. A copy of the International Application as filed (35 U.S.C. 371(c)(2)).</p> <p>a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</p> <p>b. <input type="checkbox"/> has been transmitted by the International Bureau.</p> <p>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</p> <p>6. <input type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</p> <p>b. <input type="checkbox"/> have been transmitted by the International Bureau.</p> <p>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has <b>NOT</b> expired.</p> <p>d. <input type="checkbox"/> have not been made and will not be made.</p> <p>8. <input type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (U.S.C. 371(c)(3)).</p> <p>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p>		
<p><b>Items 11. To 16. Below concern document(s) or information included:</b></p> <p>11. <input type="checkbox"/> An Information Disclosure Statement under 37 C.F.R. 1.97 and 1.98.</p> <p>12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A FIRST preliminary amendment. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</p> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input type="checkbox"/> Other items or information.</p> <p><input type="checkbox"/> This application is entitled to "Small entity" status. <input type="checkbox"/> "Small entity" statement attached.</p>		



U.S. APPLICATION NO. (If known, see 37 C.F.R. 1.51) <b>09/2786510</b> Unassigned		INTERNATIONAL APPLICATION NO. <b>PCT/NZ00/00063</b>		ATTORNEY'S DOCKET NUMBER <b>3652-33</b>	
17. <input checked="" type="checkbox"/> The following fees are submitted:				<b>CALCULATIONS</b> PTO USE ONLY	
<b>BASIC NATIONAL FEE (37 C.F.R. 1.492(a)(1)-(5):</b> -- Neither international preliminary examination fee (37 C.F.R. 1.482) nor international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO .....\$1000.00 -- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO .....\$860.00 -- International preliminary examination fee (37 C.F.R. 1.482) not paid to USPTO but international search fee (37 C.F.R. 1.445(a)(2)) paid to USPTO .....\$710.00 -- International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) .....\$690.00 -- International preliminary examination fee paid to USPTO (37 C.F.R. 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) .....\$100.00  <div style="text-align: right;"> <b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b> \$ 1,000.00         </div>					
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 C.F.R. 1.492(e)). <div style="text-align: right;">\$ 0.00</div>					
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	37	-20 = 17	X \$18.00	\$	306.00
Independent Claims	3	-3 = 0	X \$80.00	\$	0.00
MULTIPLE DEPENDENT CLAIMS(S) (if applicable)			\$270.00	\$	0.00
<b>TOTAL OF ABOVE CALCULATIONS =</b>				\$	<b>1306.00</b>
Reduction by 1/2 for filing by small entity, if applicable. Small entity status must also be asserted. (Note 37 C.F.R. 1.9, 1.27, 1.28).				\$	0.00
<b>SUBTOTAL =</b>				\$	<b>1306.00</b>
Processing fee of \$130.00, for furnishing the English Translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 C.F.R. 1.492(f)).				\$	0.00
<b>TOTAL NATIONAL FEE =</b>				\$	<b>1306.00</b>
Fee for recording the enclosed assignment (37 C.F.R. 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 C.F.R. 3.28, 3.31). \$40.00 per property				\$	40.00
Fee for Petition to Revive Unintentionally Abandoned Application (\$1240.00 - Small Entity = \$620.00)				\$	0.00
<b>TOTAL FEES ENCLOSED =</b>				\$	<b>1346.00</b>
				Amount to be: refunded	\$
				Charged	\$
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p><b>SEND ALL CORRESPONDENCE TO:</b></p> <p>NIXON &amp; VANDERHYE P.C.            1100 North Glebe Road, 8<sup>th</sup> Floor            Arlington, Virginia 22201            Telephone: (703) 816-4000</p> </div> <div style="width: 45%; text-align: center;"> <p>SIGNATURE </p> <p><b>Leonard C. Mitchard</b> NAME</p> </div> </div> <div style="display: flex; justify-content: space-between; margin-top: 20px;"> <div style="width: 45%;"> <p><b>29,009</b> REGISTRATION NUMBER</p> </div> <div style="width: 45%; text-align: right;"> <p>March 6, 2001 Date</p> </div> </div>					

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of

COWAN et al

Atty. Ref.: 3652-33

Serial No. Unassigned

Group:

Filed: March 6, 2001

Examiner:

For: METHOD AND SYSTEM FOR MEASURING CHARACTERISTICS OF AN ORGAN

\* \* \* \* \*

March 6, 2001

Assistant Commissioner for Patents  
Washington, DC 20231

Sir:

**AMENDMENT**

Please amend the above application as follows:

**IN THE CLAIMS**

Please substitute the following amended claims for corresponding claims previously presented. A copy of the amended claims showing current revisions is attached.

5. (Amended) A method as claimed in claim 1 comprising the steps of displaying one or more images to a user and superimposing on the image a representation of the intersection of the reference model with the image.

7. (Amended) A method as claimed in claim 5 wherein the user performs the step of defining one or more boundary points on the image(s).

8. (Amended) A method as claimed in claim 5 further comprising the step of calculating the volume of the subject organ or part from the estimate model.

9. (Amended) A method as claimed in claim 5 further comprising the step of calculating the mass of the subject organ or part from the estimate model.

10. (Amended) A method as claimed in claim 5 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

11. (Amended) A method as claimed in claim 5 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

12. (Amended) A method as claimed in claim 1 wherein the subject organ comprises a kidney and the characteristics measured include cortical

thickness.

17. (Amended) A system as claimed in claim 13 further comprising display means arranged to display one or more images to a user and to superimpose on the image a representation of the intersection of the reference model with the image slice.

19. (Amended) A system as claimed in claim 17 wherein the boundary guide point definition means is arranged to obtain preferred guide point positions from a user.

20. (Amended) A system as claimed in claim 17 further comprising volume calculation means arranged to calculate the volume of the subject organ or part from the estimate model.

21. (Amended) A system as claimed in claim 17 further comprising mass calculation means arranged to calculate the mass of the subject organ or part from the estimate model.

22. (Amended) A system as claimed in claim 17 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle

or part thereof.

23. (Amended) A system as claimed in claim 17 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

24. (Amended) A system as claimed in claim 17 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

29. A program as claimed in claim 25 further comprising display means arranged to display one or more images to a user and to superimpose on the image a representation of the intersection of the reference model with the image.

31. (Amended) A program as claimed in claim 29 wherein the boundary guide point definition means is arranged to obtain preferred guide point positions from a user.

32. (Amended) A program as claimed in claim 29 further comprising volume calculation means arranged to calculate the volume of the subject organ or part from the estimate model.

33. A program as claimed in claim 29 further comprising mass calculation means arranged to calculate the mass of the subject organ or part from the estimate model.

34. (Amended) A program as claimed in claim 29 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

35. (Amended) A program as claimed in claim 29 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

36. (Amended) A program as claimed in claim 29 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

37. (Amended) A computer program as claimed in claim 25 embodied on a computer readable medium.

**REMARKS**

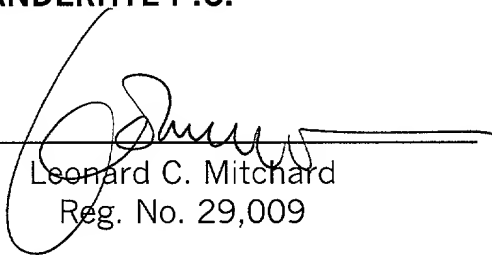
The above amendments have been made to place the application in a more traditional format.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page/s is/are captioned "**Version With Markings To Show Changes Made.**"

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By: \_\_\_\_\_

  
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## **VERSION WITH MARKINGS TO SHOW CHANGES MADE**

### **IN THE CLAIMS**

5. (Amended) A method as claimed in [any one of the preceding claims] claim 1 comprising the steps of displaying one or more images to a user and superimposing on the image a representation of the intersection of the reference model with the image.

7. (Amended) A method as claimed in claim 5 [or claim 6] wherein the user performs the step of defining one or more boundary points on the image(s).

8. (Amended) A method as claimed in [any one of the preceding claims] claim 5 further comprising the step of calculating the volume of the subject organ or part from the estimate model.

9. (Amended) A method as claimed in [any one of the preceding claims] claim 5 further comprising the step of calculating the mass of the subject organ or part from the estimate model.

10. (Amended) A method as claimed in [any one of the preceding claims] claim 5 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

11. (Amended) A method as claimed in [any one of the preceding claims] claim 5 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

12. (Amended) A method as claimed in [any one of claims 1 to 9" claim 1 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

17. (Amended) A system as claimed in [any one of claims 13 to 16] claim 13 further comprising display means arranged to display one or more images to a user and to superimpose on the image a representation of the intersection of the reference model with the image slice.

19. (Amended) A system as claimed in claim 17 [or claim 18] wherein the boundary guide point definition means is arranged to obtain preferred guide point positions from a user.

20. (Amended) A system as claimed in [any one of claims 13 to 19] claim 17 further comprising volume calculation means arranged to calculate the volume of the subject organ or part from the estimate model.

21. (Amended) A system as claimed in [any one of claims 13 to 20] claim 17 further comprising mass calculation means arranged to calculate the mass of the subject organ or part from the estimate model.

22. (Amended) A system as claimed in [any one of claims 13 to 21] claim 17 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

23. (Amended) A system as claimed in [any one of claims 13 to 22] claim 17 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

24. (Amended) A system as claimed in [any one of claims 13 to 21] claim 17 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

29. A program as claimed in [any one of claims 25 to 28] claim 25 further comprising display means arranged to display one or more images to a user and to superimpose on the image a representation of the intersection of the

reference model with the image.

31. (Amended) A program as claimed in claim 29 [or claim 30] wherein the boundary guide point definition means is arranged to obtain preferred guide point positions from a user.

32. (Amended) A program as claimed in [any one of claims 25 to 31] claim 29 further comprising volume calculation means arranged to calculate the volume of the subject organ or part from the estimate model.

33. A program as claimed in [any one of claims 25 to 32] claim 29 further comprising mass calculation means arranged to calculate the mass of the subject organ or part from the estimate model.

34. (Amended) A program as claimed in [any one of claims 25 to 33] claim 29 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

35. (Amended) A program as claimed in [any one of claims 25 to 34] claim 29 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through

changes in wall thickness over time.

36. (Amended) A program as claimed in [any one of claims 25-33] claim 29 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

37. (Amended) A computer program as claimed in [any one of claims 25 to 33] claim 25 embodied on a computer readable medium.

15/ PRTS

09/786510

JC02 Rec'd PCT/PTO 06 MAR 2001

METHOD AND SYSTEM OF MEASURING CHARACTERISTICS OF AN ORGAN

**FIELD OF THE INVENTION**

5 The invention relates to a method and system of measuring characteristics of an organ or part thereof. The method and system of the invention are particularly suited to measuring cardiac function, volume, and/or mass of a ventricle of the heart of a subject from multiple image slices obtained by magnetic resonance imaging (MRI). The method and system of the invention may also be used to calculate the volume  
10 and/or mass and other characteristics of other organs such as a lung, kidney or brain, to measure the position of the wall of a blood vessel for the purposes of analysis of flow, or to calculate the volume and/or mass of a bone, tumour or cyst.

15 **BACKGROUND TO INVENTION**

Ventricular mass, volumes and wall thickness at end diastole and end systole are essential clinical parameters for diagnosis and management of many cardiac diseases. Magnetic resonance imaging (MRI) may be used to estimate heart wall  
20 motion by reconstructing the shape and motion of the left ventricle.

MRI is also able to provide accurate and precise estimations of ventricular mass, volume and wall thickness, since it is a true 3-dimensional method which is not dependent on geometric assumptions and is not limited in the position or orientation  
25 of the possible images, unlike other methods, such as for example echocardiography or computed tomography.

Recent advances in MRI allow the acquisition of 10 to 20 MRI images or slices in short and long axis or arbitrary orientations, each with 10 to 25 frames through the  
30 cardiac cycle in real time, or ten to fifteen minutes or less, which is a clinically acceptable time. Previous studies have shown that the summation of areas outlined in short axis MRI slices gives more accurate and reproducible estimates of volume than echocardiography or LV angiography.

35 A major limitation of the MRI slice summation method is the prohibitive time required to outline the endocardial and epicardial boundaries of the left ventricle in each slice. This severely limits application of the use of the technique to routine clinical care.

In the past, many semi-automated image segmentation algorithms have been applied to this problem, but these solutions are frequently not sufficiently robust and accurate for routine clinical use. In particular the image pixel intensities are insufficient to adequately constrain the segmentation problem, due to the limited temporal and spatial resolution, presence of image artifacts, and lack of contrast between blood and muscle. The amount of time spent on manual editing and correction of contours obtained from these previous solutions renders automated methods nearly as slow as manual contouring in clinical practice.

Other techniques apply model fitting techniques to estimate characteristics of organs such as the left ventricle. T McInerney and D Terzopoulos in "A Dynamic Finite Element Surface Model for Segmentation and Tracking in Multidimensional Medical Images with Application to Cardiac 4D Image Analysis", Computerized Medical Imaging and Graphics 19:69-83; 1995 describe a deformable "balloon" model that is topologically isomorphic to a sphere for use in estimating volume and motion of the left ventricle. PCT international patent publication WO 99/18450 to Philips AB titled "Method of and Device for Imaging an Object by means of Magnetic Resonance" describes the use of an ellipsoid to model the left ventricle. Both techniques require the use of edge detection algorithms and in doing so suffer from the disadvantages discussed above.

#### **SUMMARY OF INVENTION**

In broad terms in one aspect the invention comprises a method of measuring characteristics of an organ or part thereof of a subject from multiple images of the subject's organ or part thereof, the method comprising the steps of defining the spatial position of at least two of the slices; defining a reference model of the organ or part thereof scaled according to the distance between the slices; defining one or more boundary guide points associated with one or more slices for which the spatial positions have been defined; converting the guide points to three-dimensional coordinates; defining an estimate model by fitting the reference model to the guide points; and calculating the characteristics from the estimate model.

In broad terms in another aspect, the invention comprises a system for measuring characteristics of an organ or part thereof of a subject from multiple image slices of the subject's organ or part thereof, the system comprising a memory in which is stored the spatial position of at least two of the slices; reference model definition

means arranged to define a reference model of the organ or part thereof scaled according to the distance between the slices; boundary guide point definition means arranged to define one or more boundary guide points associated with one or more slices for which the spatial positions are stored in the memory; conversion means  
5 arranged to convert the guide points to three-dimensional coordinates; estimate model definition means arranged to define an estimate model by fitting the reference model to the guide points; and calculation means arranged to calculate the characteristics from the estimate model.

10 In yet another form the invention comprises a computer program for measuring characteristics of an organ or part thereof of a subject from multiple image slices of the subject's organ or part thereof, the program comprising storage means arranged to store the spatial position of at least two of the slices; reference model definition means arranged to define a reference model of the organ or part thereof scaled  
15 according to the distance between the slices; boundary guide point definition means arranged to define one or more boundary guide points associated with one or more slices for which the spatial positions are stored in the memory; conversion means arranged to convert the guide points to three-dimensional coordinates; estimate model definition means arranged to define an estimate model by fitting the reference  
20 model to the guide points; and calculation means arranged to calculate the characteristics from the estimate model.

#### **BRIEF DESCRIPTION OF THE FIGURES**

25 Preferred forms of the invention will now be described, by way of example, with reference to the accompanying figures in which:

Figure 1 is a flow chart outlining a preferred form of the method of the invention;

30 Figure 2 shows the main window of a preferred form of an application program in which the invention is implemented;

Figure 3 shows a guide points window and the preferred method of selecting the left ventricular basal slice from this window;

35 Figure 4 shows the preferred method of selecting the left ventricular apical slice from the window of Figure 3;



Figure 5 shows the preferred method of entering characteristics of the right ventricle from the window of Figure 3;

Figure 6 shows the preferred method of defining the base or mitral valve plane from the window of Figure 3;

Figures 7 to 10 illustrate a method of selecting boundary guide points from the window of Figure 3;

Figures 11 and 12 show a preferred window for viewing the model; and

Figures 13 to 15 show preferred displays of data obtained from the method and system of the invention.

## **DETAILED DESCRIPTION OF PREFERRED FORMS**

Figure 1 sets out a preferred form of method of the invention.

A number of images are first obtained of the left ventricle of a subject as indicated at 110. The images could be acquired from an MRI scanner, or may alternatively be acquired by an ultra-fast CT, 3-dimensional ultrasound machine or echocardiography, or other suitable imaging modality. The images could also be obtained from confocal microscopy, electron microscopy or histology. The images are typically 2-dimensional cines or movies of the heart and are taken at standard orientations, for example, short axis and long axis, or at entirely arbitrary positions depending on the nature of the pathology and imaging modality.

The preferred images are acquired in a number of spatial locations, having a lowest or apical slice, a highest or basal slice, one or more middle slices and one or more long axis slices. The preferred images are acquired in between 2 and preferably 20 spatial locations, and typically 12 spatial locations. Preferably images in each of these spatial locations are obtained at multiple frames through the cardiac cycle. The preferred number of frames is 10 to 25.

Conventional MRI imaging apparatus produces images having image headers. The image header in each image generally comprises an extensive data list including patient name and scan parameters at the beginning of each image. The image

header also provides data representing the spatial position and temporal position of each slice or frame.

5 The images are loaded into memory as indicated at 112. The preferred memory forms part of a computer having a CPU, input devices and a display device such as a VDU. The preferred input devices comprise a keyboard, mouse and disk drive, typically a networked magneto-optical disc drive and/or CD ROM drive. Images may also be transferred over a network. The preferred memory comprises a hard disk drive suitable for storing the images.

10

The preferred computer comprises a SUN SparcStation, SGI work station, PC, or similar having at least 128 MB Ram or similar. The computer has loaded on it suitable operating system software, such as SOLARIS, IRIX, WINDOWS or LINUX. The preferred computer is arranged to execute application software in which the present invention has been developed. The preferred application software is written in C++, using OpenGL, OpenInventor and Xwindows for graphical interfaces.

Referring to Figure 2, the user is presented with a main window from which a number of options may be selected. The option to load planes is indicated at 14 which loads the three-dimensional position of the images and the option to load frames is indicated at 15 which loads the position of the images in time. This spatial and temporal information is generally included in the image headers. The option to load images is indicated at 16. Each separate image location is displayed in a second window at the first phase of imaging simultaneously.

25

Various parameters may be specified by the user at the time of loading the images, for example Model Type, Fit Type and Data Set. The user may also specify directory names for directories such as a Data Directory, a Model Directory and a Script Directory.

30

As shown at 114 in Figure 1, the next step is to define a three-dimensional coordinate system from two or more of the slices for which the spatial positions have been defined. The main window of Figure 2 presents to the user an option to enter the guide points editor. The guide points editor loads the editor window shown in Figure 3. The editor window includes panel 20 which in the preferred form displays thumbnail images of the images stored in the memory. Panel 22 displays an enlarged image of one of the images displayed in panel 20. The preferred form window shown in Figure 3 also provides the user with the ability to zoom and pan

35

images and to adjust brightness and contrast. The user may select the image to be displayed in panel 22 by, for example, clicking on one of the thumbnails displayed in panel 20.

5 The user first selects the basal or highest short axis slice in panel 20, clicking on the thumbnail image to display the enlarged image in panel 22. In Figure 3 the user has selected the basal slice which is described below panel 22 as the seventh short axis image obtained during the first time interval or frame.

10 The user selects the Base option indicated at 24. A prompt is displayed for the user to pick a point to represent the base in the model's cardiac coordinate system. The user selects a point in the centre of the ventricular image by clicking in panel 22. Once the desired base has been selected the user selects the option to accept the base indicated at 26.

15 Referring to Figure 4, the user repeats the procedure to select the apex of the object. The user selects the Apex option indicated at 28. A prompt is displayed for the user to pick a point representing the apex and the user then selects the point in panel 22. Once the desired apex has been selected the user accepts the apex as indicated at  
20 30.

If the spatial position of the basal slice and the apical slice is known then land marks may be determined, for example the long axis. The software calculates the length and position of the long axis by defining a line in 3-dimensional space between the  
25 two points selected by the user.

As shown in Figure 5, the user is not limited to defining the co-ordinate system on the left ventricle. By selecting the option indicated at 35 the user may select different points or landmarks to analyse, for example, the right ventricle.

30 As shown in Figure 6, the user may display in panel 22 an image taken of the long axis of the object, as indicated by the description below panel 22. The user selects the Base Points option 32 which then prompts the user to choose two or more points on the image to define the maximum extent for estimate model and calculate  
35 volumes of, for example, the mitral valve plane. The user selects the points by clicking in panel 22 and once the desired points have been selected the user accepts the base points indicated at 34. Further options may also be provided, for example advancing the image displayed in panel 22 to the next frame.

It will be appreciated that the user does not need to define the axis by selecting the centre of the ventricle in the basal and apical slices. The user may instead define the centre of the left ventricle in two slices which are not the basal or apical slices. The software may then calculate the position of the long axis by defining a line in 3-dimensional space between these two points. The length of the long axis of the left ventricle may then be calculated separately from the distance between the basal and apical slices if the spatial position of the slices is known.

As shown at step 116 in Figure 1, the software defines a reference model of a left ventricle. The preferred reference shape closely approximates the generic shape of a left ventricle. The reference model may be constructed from real patient data, but does not have to be absolutely accurate in terms of an individual patient. The reference model may be defined as an analytical function, as a coordinate system, or as data points.

The preferred reference model is a finite element model consisting of at least 16 elements, typically 16 to 40, each with cubic interpolation in the circumferential and longitudinal directions. Linear interpolation is used to couple the endocardial and epicardial surfaces into a coherent 3-D model. The preferred model is defined in a polar coordinate system in which the radial coordinate of the model is fitted as a function of the two angular coordinates in the circumferential and longitudinal directions respectively. The preferred initial shape of the reference model is a regular ellipsoid, typically a prolate spheroid, obtained by setting the endocardial and epicardial surfaces to a constant radial value. The preferred reference model is scaled according to the length of the long axis of the left ventricle of the subject with the extent of the model in the longitudinal direction set to correspond to the point identified on the most basal slice of the left ventricle in the long axis.

The preferred estimate model is obtained by a least squares finite element modelling process in which the left ventricle is divided into a number of rectangular segments or elements. Each element defines a bicubic spline surface for part of the endocardial and epicardial surfaces of the left ventricle. It is important to ensure continuity in the surface defined by adjacent elements. To ensure continuity, adjacent elements are constrained to have the same position and slope on each side of the join. Ensuring continuity in this way eliminates or at least reduces ridges and sharp transitions between adjacent elements.

Within each element, the geometric coordinate field  $\mathbf{x}$  is given as a function of element or material coordinates  $\xi$  by a weighted average of nodal values:

$$\mathbf{x}(\xi_1, \xi_2, \xi_3) = \sum_n \Psi_n(\xi_1, \xi_2, \xi_3) \lambda^n \quad (1)$$

where  $\lambda^n$  are the nodal values,  $\Psi_n$  are the element basis functions which give the relative weighting of each nodal value, and  $(\xi_1, \xi_2, \xi_3)$  are the element co-ordinates.

- 10 The geometric field  $\lambda$  is defined to be the radial co-ordinates in the polate spheroidal co-ordinate system:

$$\begin{aligned} x &= f \cosh(\lambda) \cos(\mu) \\ y &= f \sinh(\lambda) \sin(\mu) \cos(\theta) \\ z &= f \sinh(\lambda) \sin(\mu) \sin(\theta) \end{aligned} \quad (2)$$

- 15 where  $(\lambda, \mu, \theta)$  are the radial, longitudinal and circumferential co-ordinates of the polar system and  $(x, y, z)$  are the corresponding rectangular cartesian co-ordinates. The focal length  $f$  of the polate system is preferably chosen so that the  $\lambda=1$  surface gives a good initial approximation of the left ventricular epicardial surface, providing an overall scale factor for the ventricle.

- 20 Previously defined points are used to determine the initial position of the model with respect to the images. These are:

- 25 a) the location of the central axis at the center of the LV in an apical short axis image  
b) the location of the central axis at the center of the LV in a basal short axis image  
c) the approximate centroid of the right ventricle  
d) a set of points describing the mitral valve plane.

- 30 A model-based coordinate system is then constructed with the origin placed on the central axis of the LV one third of the distance from the base to the apex. Nodes are placed at equally spaced intervals in the two angular coordinates  $(\mu, \theta)$  and at a constant radial coordinate  $(\lambda)$ . The centroid of the RV has  $\theta=0$  and the extent of the model in the  $\mu$  direction is governed by the basal margin points. The distance from

apex to base is used to determine the focal length of the prolate system and provides an overall scale factor for the LV.

Each guide point is projected onto the model along lines of constant  $\mu$  and  $\theta$  and only  
5 the  $\lambda$  field is fitted by linear least squares.

As shown at 118 in Figure 1, the next step is to define one or more guide points on one or more slices for which the spatial positions have been defined. Referring to Figure 7 the user is presented with the option indicated at 38 of defining guide  
10 points. The user then selects and displays in panel 22 any one of the slices stored in the memory. The image of the subject organ is displayed in panel 22. A representation of the reference model is preferably superimposed on the image of the subject organ. In the preferred form, a representation of the intersection of the reference model with the image slice superimposed on the image slice, as indicated  
15 by contour lines 39A and 39B.

The user first selects the active surface which is being defined as indicated at 40. In Figure 8 the user has selected the left ventricular endocardial boundary as the active surface. Using a mouse, the user defines one or more boundary guide points on the  
20 selected slice by clicking in panel 22. These guide points, in combination with the reference model, define the endocardial or epicardial boundaries of the heart. Preferably three to four endocardial boundary guide points and three to four epicardial boundary guide points are entered for each slice, although the user is able to enter a large number of boundary guide points for a particular slice or may  
25 instead ignore a slice and enter no boundary guide points for it.

As the user defines the guide points, the system converts these guide points to three-dimensional coordinates from the image position in space for each boundary guide point, and fits the model by forcing the model to adhere closely to the guide points,  
30 as will be discussed below.

Where a number of image frames are stored in memory, the user may advance to the next frame by clicking on the Next Frame option indicated at 43.

35 Figures 9 and 10 further illustrate the process by which the boundary points are defined by the user. The user is defining the endocardial boundary of an image slice different to the one shown in Figure 7. In Figures 9 and 10 the user is defining the epicardial and endocardial boundaries respectively for a further image.

It will be appreciated that where an organ other than the left ventricle is to be modelled, the reference model will be varied. For example, where the invention is used to model the right ventricle, lung and/or kidney, a different reference model will be defined.

The next step indicated at 120 in Figure 1 is to form an estimate model by fitting the reference model to the guide points. This process could be initiated automatically whenever the user selects the Next Frame option indicated at 43 in Figures 7 to 10, or may be updated automatically in real time with the insertion or deletion of a guide point or any change in guide point position.

The preferred method for incorporating the reference model data is to minimise an error function consisting of the sum of a smoothing term and a term penalising the distance between each boundary guide point and the corresponding reference model position.

The preferred smoothing term penalises changes in slope and curvature around the left ventricle, allowing the reference model to realistically interpolate guide point data where the data is sparse.

The preferred penalty is introduced into the least squares method which penalises only the sum of the squared deviations from the boundary guide points to the reference model surface. In particular, the first and second derivatives of the surfaces are constrained to be minimised within the least squares fit to prevent rippling and other abnormalities. In this sense, the smoothing can be viewed as weighting the estimate model more toward the reference model than the boundary guide points so that the reference model is imposed more strongly where there are no or insufficient boundary guide points.

One preferred smoothing method is set out more particularly below, in which the error function minimised is:

$$E = S(\lambda) + \sum_g (\lambda(\xi_g) - \lambda_g)^2 \quad (3)$$

where  $\lambda_g$  are the positions of the guide point data and  $\lambda(\xi_g)$  are the model positions at element co-ordinates  $\xi_g$  corresponding to  $\lambda_g$ . The element co-ordinates are preferably found by projecting the guide data onto the model along lines of constant

$\mu$  and  $\theta$ .  $S(\lambda)$  denotes a smoothing term included in the error function to constrain the model to smoothly interpolate between the sparse guide points.

$S(\lambda)$  is preferably a weighted Sobolev norm which penalizes the displacement of the estimate model from the reference model.

$$S(\lambda) = \int_{\Omega} \alpha_1 \left[ \frac{\partial u}{\partial \xi_1} \right]^2 + \alpha_2 \left[ \frac{\partial u}{\partial \xi_2} \right]^2 + \beta_1 \left[ \frac{\partial^2 u}{\partial \xi_1^2} \right]^2 + \beta_2 \left[ \frac{\partial^2 u}{\partial \xi_2^2} \right]^2 + \gamma_1 \left[ \frac{\partial^2 u}{\partial \xi_1 \partial \xi_2} \right]^2 + \gamma_2 \left[ \frac{\partial^2 u}{\partial \xi_1 \partial \xi_3} \right]^2 + \gamma_3 \left[ \frac{\partial^2 u}{\partial \xi_2 \partial \xi_3} \right]^2 d\Omega \quad (4)$$

where  $u = \lambda - \lambda^*$  where  $\lambda^*$  is the reference model. The weights  $\alpha_1$  and  $\alpha_2$  penalize the slope of the displacement field in the circumferential and longitudinal directions respectively, the weights  $\beta_1$  and  $\beta_2$  penalize curvature and the weights  $\gamma_1$ ,  $\gamma_2$  and  $\gamma_3$  couple slopes between directions. Typical smoothing weights are  $\alpha_1 = \alpha_2 = 0$ ,  $\beta_1 = \beta_2 = 0.001$ ,  $\gamma_1 = \gamma_2 = \gamma_3 = 0.01$ .

The resulting estimate model incorporates endocardial and epicardial boundary guide points, the long axis of the left ventricle, reference model data and smoothing constraints to produce endocardial and epicardial left ventricular surfaces in three or four dimensions closely approximating the true surfaces represented in the images.

Having defined these surfaces, the software may then calculate the intersection of the image slices with the surfaces and display the estimate model as indicated at 122 in Figure 1. The intersections are each represented by two lines, one line representing the endocardium and the other line representing the epicardium which are close to the edges on the images.

Having calculated endocardial and epicardial surface boundaries on each image, image(s) are then evaluated, preferably by the user, for acceptable contours as indicated at 124 and acceptable image quality as indicated at 126. The software may then perform local image processing as indicated at 128 to further improve the quality of the left ventricle boundary edges displayed in the images. The use of local image processing is not essential to the invention. Where provided, it may be invoked by the user. An edge is characterized by an abrupt change in intensity



indicating a boundary, and is called a discontinuity. In general an edge is often seen as a slow change in grey level values between connected pixels. While a boundary edge may be readily apparent to the human eye, it can be difficult for software to detect.

5

Prior art methods of detecting discontinuities or edges include running a mask or window over the image, or by applying a known edge enhancing filter such as a Roberts, Sobel or Laplacian operator. Applying such a filter to an entire image in order to find boundary edges is computationally expensive.

10

Using the present invention, the endocardial and epicardial boundaries have been estimated with the estimate model. The software therefore can calculate the likely position of a boundary edge in an image. An *a priori* technique may then be applied to guide the search for the boundary in the image.

15

In one method, radial lines may be drawn extending through both the endocardial and epicardial boundaries. An edge filter may be applied at the intersection of these boundaries and the radial line to determine the points on the radial line most likely to represent the endocardial and epicardial edges.

20

Further local processing could also include thresholding, for example grey-scale thresholding. All pixel values falling between two threshold values  $T_1$  and  $T_2$  retain their grey-scale values but all pixel values outside this interval are set to zero. Such multiple thresholds may be applied to reduce the number of grey-level values in an image, thereby enhancing the contrast. Thresholding may be applied, for example, to contrast the area in the image inside the endocardial boundary, from the area between the endocardial and epicardial boundaries, and/or the area outside the epicardial boundary.

25

Local image processing and thresholding as described above may generate additional data points which may be added to the existing boundary guide points. The estimate model contour may then be redefined based on the additional data points so that the relationship to the actual images is improved.

30

The additional data points obtained from local image processing and thresholding may be assigned less weight than boundary guide points selected by the user, as it will be appreciated that these additional data points may be less reliable than those selected by the user. The generated data points may be displayed to the user in

35

order to identify where additional guide points are needed to improve the estimate model, for example, where a contour has missed the actual edge.

It will be appreciated that where image processing is performed, it is performed at a local level. It is assumed that the edge is in a particular region. Image processing is computationally expensive and in the past has been performed on an entire image or slice. Using the invention, it is possible to determine the approximate position of the region so that image processing can be concentrated on that region, significantly reducing the processing time. Where the local image processing is unable to determine the location of an edge, the estimate model will be determined primarily from the guide points defined by the user, the reference model, and smoothing parameters.

The software may then define the final estimate model surfaces from the finite element modelling process, with the inclusion of data points obtained by local image processing. The intersection of this surface with the image slices permits the software to display on the original images the left ventricular endocardial and epicardial boundary walls. The step of drawing the estimate model is indicated in Figure 1 at 122.

The number of guide points can be reduced substantially if the images are of good quality and the image processing is able to accurately define the edges and guide the estimate model on to them.

As shown in Figure 2, the main window presents to the user the option of viewing the images in three dimensions, indicated at 54. On selecting this option the user is presented with a 3D viewer window as will be more particularly described with reference to Figures 11 and 12.

Referring to Figure 11, the window includes panel 56 in which images are displayed. The user has the option of selecting image planes as the desired view as indicated at 124. Where the Image planes option is selected, the user may select which image slices to display in panel 56. In Figure 11 the user has selected the long axis slice and the fifth short axis slice to display in panel 56. Also displayed in panel 56 are the intersections of the estimate model with the original image planes.

Referring to Figure 12, the user has elected not to display image planes. The image displayed in panel 56 is instead the estimate endocardial surface rather than individual image planes.

- 5 Each boundary or contour is then assessed by the user for appropriateness. If the boundary or contour is unacceptable, the user may define further boundary guide points until such time as the boundary or contour is acceptable, as indicated in Figure 1 at 124.
- 10 Left ventricular cardiac volume, for example, may then be estimated by calculating the volume bounded by the estimate model in the step indicated at 130 in Figure 1. Left ventricular wall thickness may also be calculated from the estimate model. Left ventricular mass may be calculated from the difference between the volumes enclosed by the endocardial and epicardial contours multiplied by an appropriate
- 15 constant, for example 1.05 g/ml.

- It will be appreciated that the volume, wall thickness and mass of the right ventricle may also be calculated in the same way. Where more than one frame is stored in the memory, the method may be used to measure abnormalities in the left or right
- 20 ventricle identified through changes in wall thickness over time. The system may also be arranged to calculate area, curvature, angles and other parameters from the estimate model.

- The method and system of the invention may further provide the results of
- 25 measurement and analysis in an intuitive, useful and interactive way that the cardiologist can understand and use in patient management. Referring to Figure 13, the system may display to a user the volumes of blood or muscle associated with each imaging slice. These volumes are preferably determined by calculating the area of the endocardium or epicardium from the estimate model for each slice and
- 30 multiplying each area by the slice thickness.

- Individual slice identifiers are indicated at 80 in a display panel. By clicking in the appropriate box adjacent a slice identifier the user may view a graph indicated at 82
- 35 of volume vs time for the mass, endocardium or epicardium respectively. Individual boxes indicated at 84 may display numerical values for end-diastolic and end-systolic volumes, mass, stroke volume and ejection fraction for each slice.

Figure 14 illustrates display of data similar to the data of Figure 13. In Figure 14 regions or sections of the ventricle are displayed according to the standard definitions of the American Society of Echocardiographers. The data displayed in Figure 14 is useful to a cardiologist as the data is independent of the original scan planes. The data has been acquired by mathematically sampling the model in each of the regions.

Figure 15 illustrates a further display in which the left ventricle has been folded out onto a flat surface and the wall thickness at every point mapped in a different colour or shade. This display cines through the cardiac cycle as wall thickness changes. Arbitrary user defined regions can be drawn onto the map and the results shown as a graph, for example regions A, B and C in Figure 14. The right ventricle insertion with the left ventricle is shown by the dots in the image of the left ventricle. Further buttons on the display switch different parts of the display on and off.

The method may also be used to measure characteristics of other organs for example the lung, the kidney or may be used to measure the wall of a blood vessel. In the case of a kidney the method may be used to measure cortical thickness.

In a further form the invention could be implemented on or associated with scanning apparatus. As the scanner produces images, an operator could insert guide points and update the estimate model. Areas of insufficient data could be identified automatically and the scanner directed to scan these planes automatically.

The method and system of the invention are particularly suited to measuring characteristics of human subjects. It will be appreciated that the same method and system could be used to measure characteristics of organs of other mammals for example rodents, canines and primates. The same technique could also be applied to the task of measuring the size and/or geometry of a cell.

The foregoing describes the invention including preferred forms thereof. Alterations and modifications as will be obvious to those skilled in the art are intended to be incorporated within the scope hereof as defined by the accompanying claims.

**CLAIMS**

1. A method of measuring characteristics of an organ or part multiple images of the organ or part thereof, the method comprising the steps of
- defining the spatial position of at least two of the images;
  - defining a reference model of the organ or part thereof scaled the distance between reference markers on the images;
  - defining one or more boundary guide points associated with images for which the spatial positions have been defined;
  - converting the guide points to three-dimensional coordinates;
  - defining an estimate model by fitting the reference model to the guide points;
  - and
  - calculating the characteristics from the estimate model.
2. A method as claimed in claim 1 wherein the distance between the reference markers is calculated by the steps of defining a point on each of two images; defining a reference line in 3-dimensional space between the points; and calculating the distance as a function of the length of the reference line.
3. A method as claimed in claim 2 wherein the reference model comprises a mathematically defined reference model defined in a polar coordinate system.
4. A method as claimed in claim 3 wherein the reference model comprises an ellipsoid having the reference line as a central axis and one or more surface points, each surface point specified by a radial distance from the central axis.

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5. A method as claimed in any one of the preceding claims comprising the steps of displaying one or more images to a user and superimposing on the image a representation of the intersection of the reference model with the image.

6. A method as claimed in claim 5 further comprising the step of performing image processing on one or more of the images.

7. A method as claimed in claim 5 or claim 6 wherein the user performs the step of defining one or more boundary points on the image(s).

8. A method as claimed in any one of the preceding claims further comprising the step of calculating the volume of the subject organ or part from the estimate model.

9. A method as claimed in any one of the preceding claims further comprising the step of calculating the mass of the subject organ or part from the estimate model.

10. A method as claimed in any one of the preceding claims wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

11. A method as claimed in any one of the preceding claims wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness *over time*.

12. A method as claimed in any one of claims 1 to 9 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

13. A system for measuring characteristics of an organ or part thereof of a subject from multiple images of the subject's organ or part thereof, the system comprising:

a memory in which is stored the spatial position of at least two of the images;

reference model definition means arranged to define a reference model of the organ or part thereof scaled according to the distance between the reference markers on the images;

boundary guide point definition means arranged to define one or more boundary guide points associated with one or more images for which the spatial positions are stored in the memory;

conversion means arranged to convert the guide points to three-dimensional coordinates;

estimate model definition means arranged to define an estimate model by fitting the reference model to the guide points; and

calculation means arranged to calculate the characteristics from the estimate model.

14. A system as claimed in claim 13 wherein the reference model definition means is arranged to calculate the distance between the reference markers by the steps of defining a point on each of two images; defining a reference line in 3-dimensional space between the points; and calculating the distance as a function of the length of the reference line.

15. A system as claimed in claim 14 wherein the reference model comprises a finite element model defined in a polar coordinate system.

16. A system as claimed in claim 15 wherein the reference model comprises an ellipsoid having the reference line as a central axis and one or more surface points, each surface point specified by a radial distance from the central axis.

17. A system as claimed in any one of claims 13 to 16 further comprising display means arranged to display one or more images to a user and to superimpose on the image a representation of the intersection of the reference model with the image slice.

18. A system as claimed in claim 17 further comprising image processing means arranged to perform image processing on one or more of the images.

19. A system as claimed in claim 17 or claim 18 wherein the boundary guide point definition means is arranged to obtain preferred guide point positions from a user.

20. A system as claimed in any one of claims 13 to 19 further comprising volume calculation means arranged to calculate the volume of the subject organ or part from the estimate model.

21. A system as claimed in any one of claims 13 to 20 further comprising mass calculation means arranged to calculate the mass of the subject organ or part from the estimate model.



22. A system as claimed in any one of claims 13 to 21 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

23. A system as claimed in any one of claims 13 to 22 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

24. A system as claimed in any one of claims 13 to 21 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

25. A computer program for measuring characteristics of an organ or part thereof of a subject from multiple images of the subject's organ or part thereof, the program comprising:

storage means arranged to store the spatial position of at least two of the images;

reference model definition means arranged to define a reference model of the organ or part thereof scaled according to the distance between the reference markers on the images;

boundary guide point definition means arranged to define one or more boundary guide points associated with one or more images for which the spatial positions are stored in the memory;

conversion means arranged to convert the guide points to three-dimensional coordinates;

estimate model definition means arranged to define an estimate model by fitting the reference model to the guide points; and

calculation means arranged to calculate the characteristics from the estimate model.

26. A program as claimed in claim 25 wherein the reference model definition means is arranged to calculate the distance between the images by the steps of defining a point on each of two images; defining a reference line in 3-dimensional space between the points; and calculating the distance as a function of the length of the reference line.

27. A program as claimed in claim 26 wherein the reference model comprises a finite element model defined in a polar coordinate system.

28. A program as claimed in claim 27 wherein the reference model comprises an ellipsoid having the reference line as a central axis and one or more surface points, each surface point specified by a radial distance from the central axis.

29. A program as claimed in any one of claims 25 to 28 further comprising display means arranged to display one or more images to a user and to superimpose on the image a representation of the intersection of the reference model with the image.

30. A program as claimed in claim 29 further comprising image processing means arranged to perform image processing on one or more of the images.

31. A program as claimed in claim or claim 30 wherein the boundary guide point definition means is arranged to obtain preferred guide point positions *from a user*.

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32. A program as claimed in any one of claims 25 to 31 further comprising volume calculation means arranged to calculate the volume of the subject organ or part from the estimate model.

33. A program as claimed in any one of claims 25 to 32 further comprising mass calculation means arranged to calculate the mass of the subject organ or part from the estimate model.

34. A program as claimed in any one of claims 25 to 33 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular mass, endocardial volume and/or wall thickness of all of the ventricle or part thereof.

35. A program as claimed in any one of claims 25 to 34 wherein the subject organ comprises a ventricle of the heart and the characteristics measured include ventricular abnormalities identified through changes in wall thickness over time.

36. A program as claimed in any one of claims 25 to 33 wherein the subject organ comprises a kidney and the characteristics measured include cortical thickness.

37. A computer program as claimed in any one of claims 25 to 35 embodied on a computer readable medium.

**ABSTRACT**

The invention provides a method of measuring characteristics of an organ or part thereof from multiple images of the organ or part thereof, the method comprising the

5 steps of defining the spatial position of at least two of the images; defining a reference model of the organ or part thereof scaled according to the distance between reference markers on the images; defining one or more boundary guide points associated with one or more images for which the spatial positions have been defined; converting the guide points to three-dimensional coordinates; defining an

10 estimate model by fitting the reference model to the guide points; and calculating the characteristics from the estimate model. The invention also provides a system and a computer program for measuring characteristics of an organ or part thereof of a subject from multiple images of the subject's organ or part thereof.

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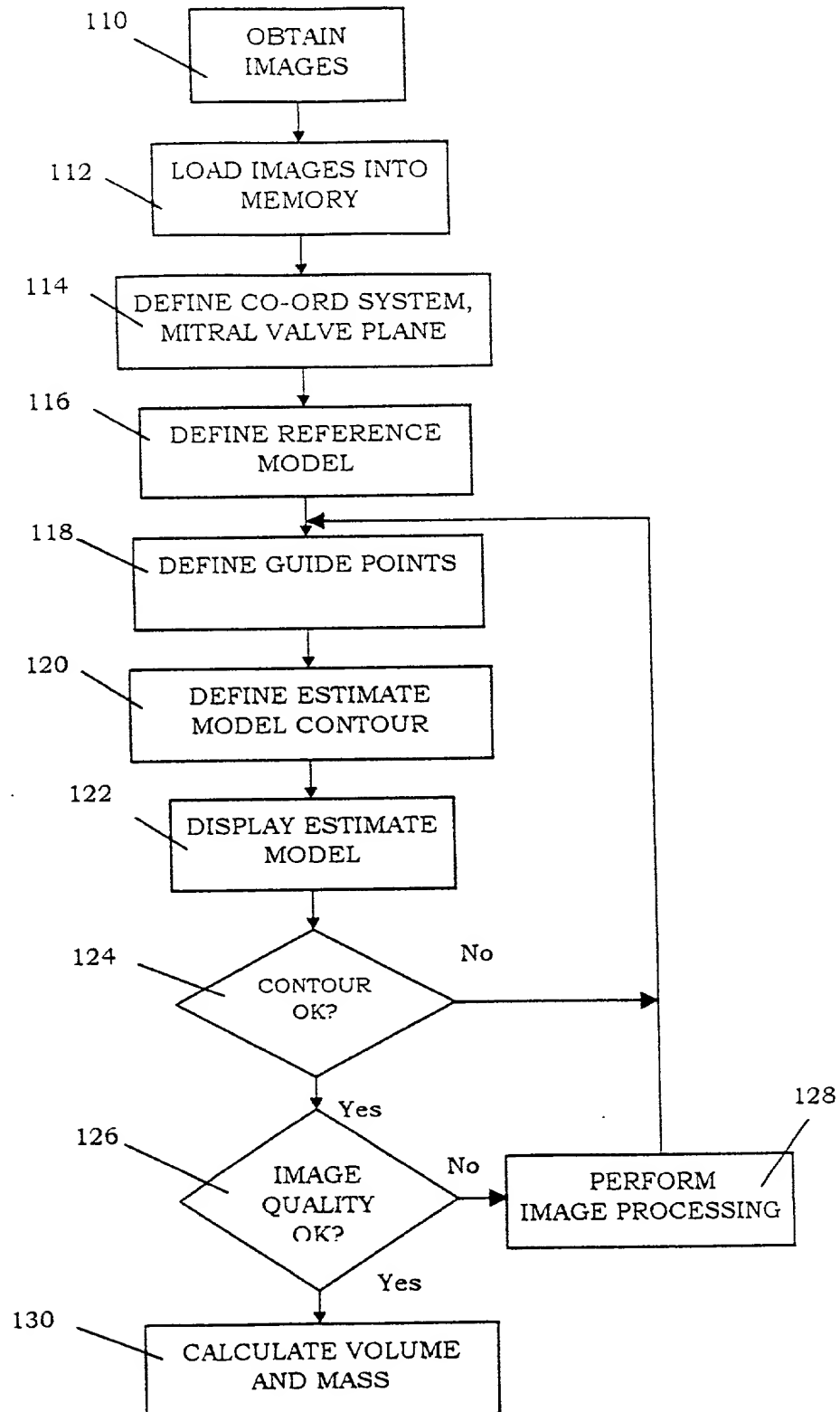


FIGURE 1

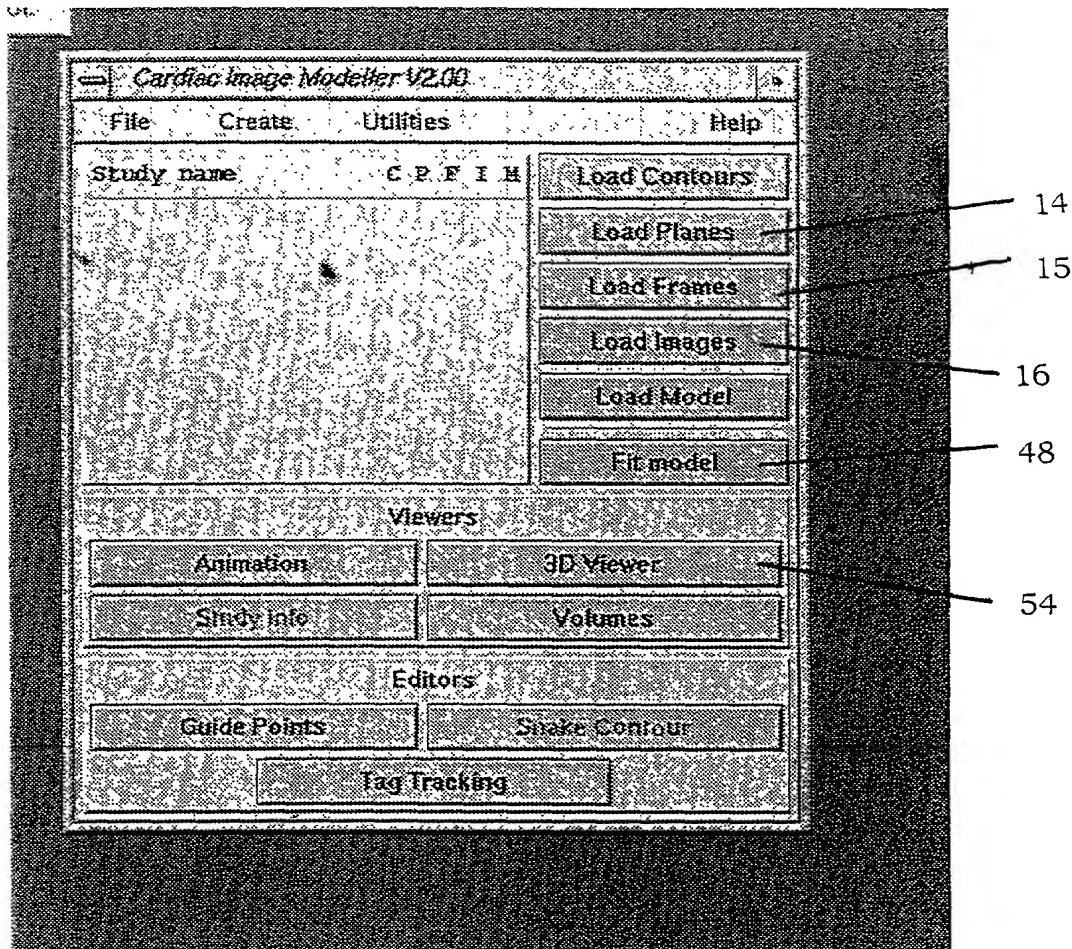


FIGURE 2

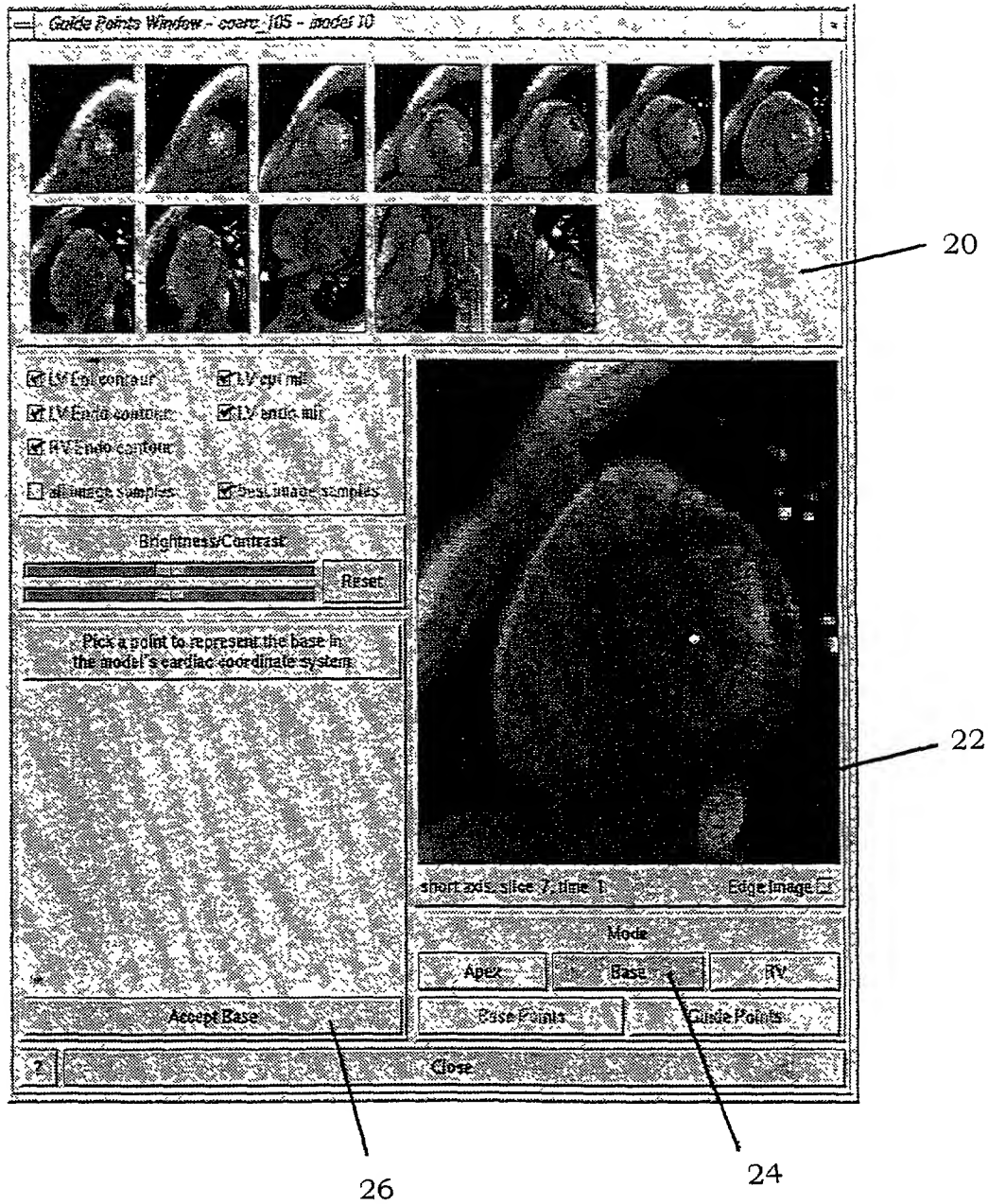


FIGURE 3

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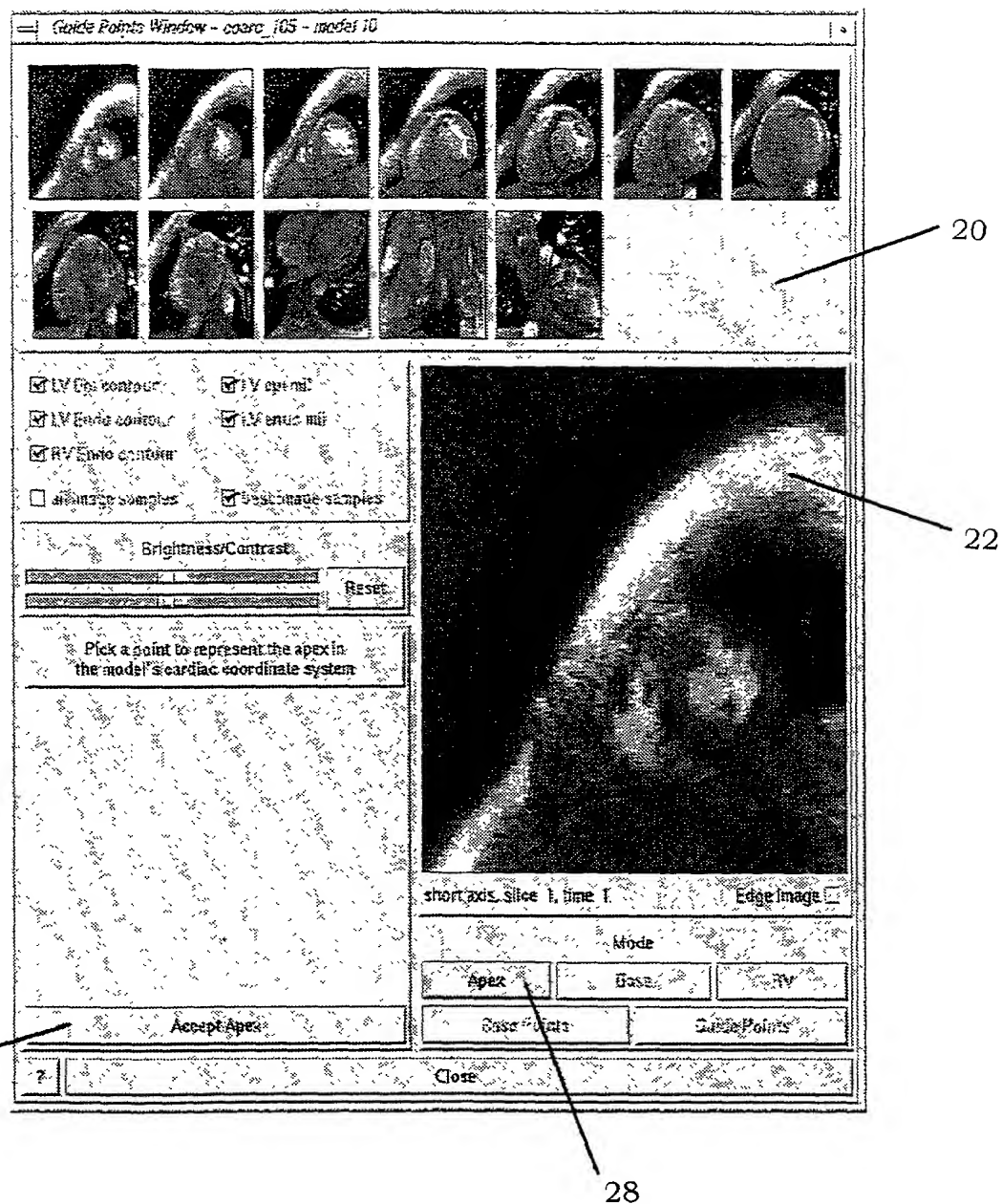


FIGURE 4



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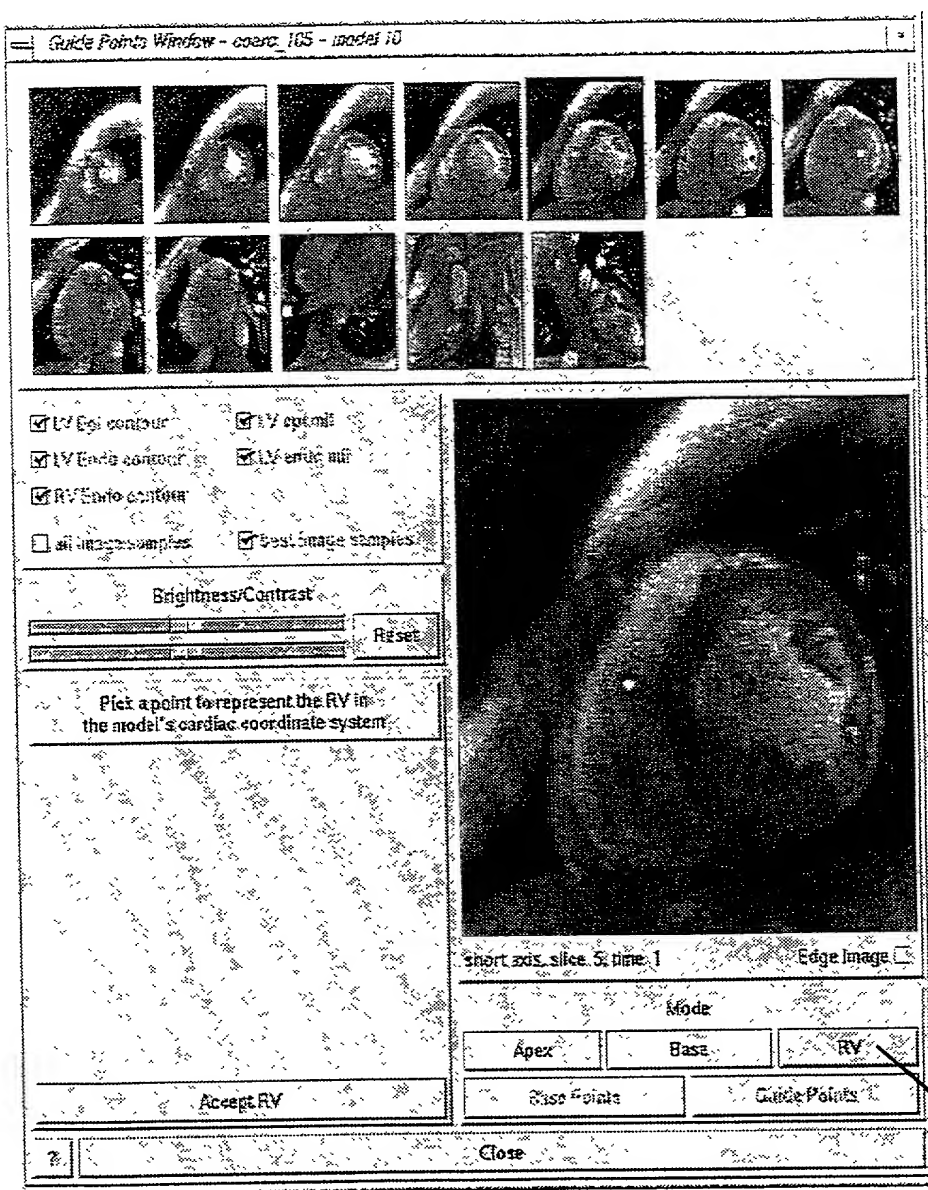


FIGURE 5

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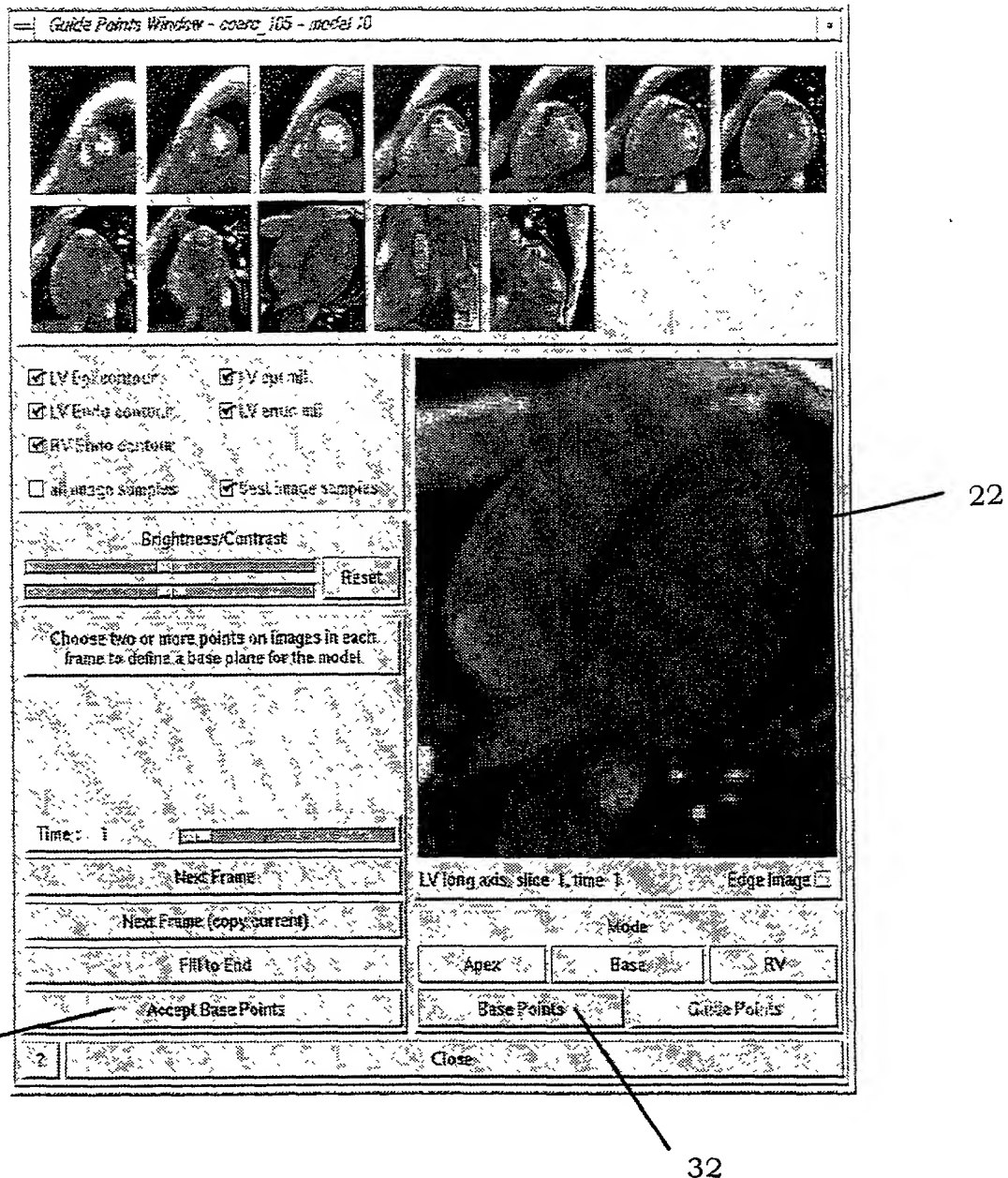


FIGURE 6

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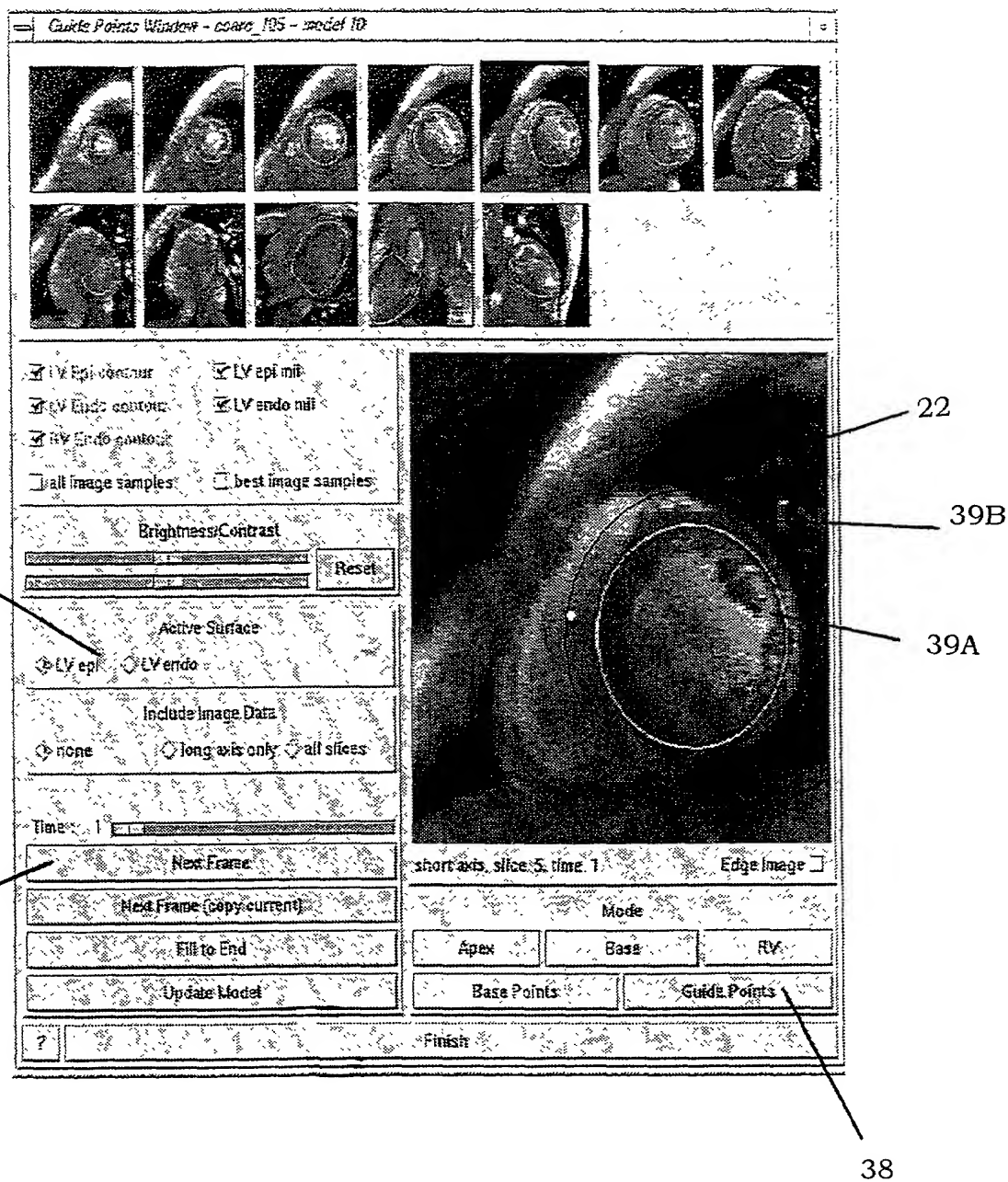


FIGURE 7

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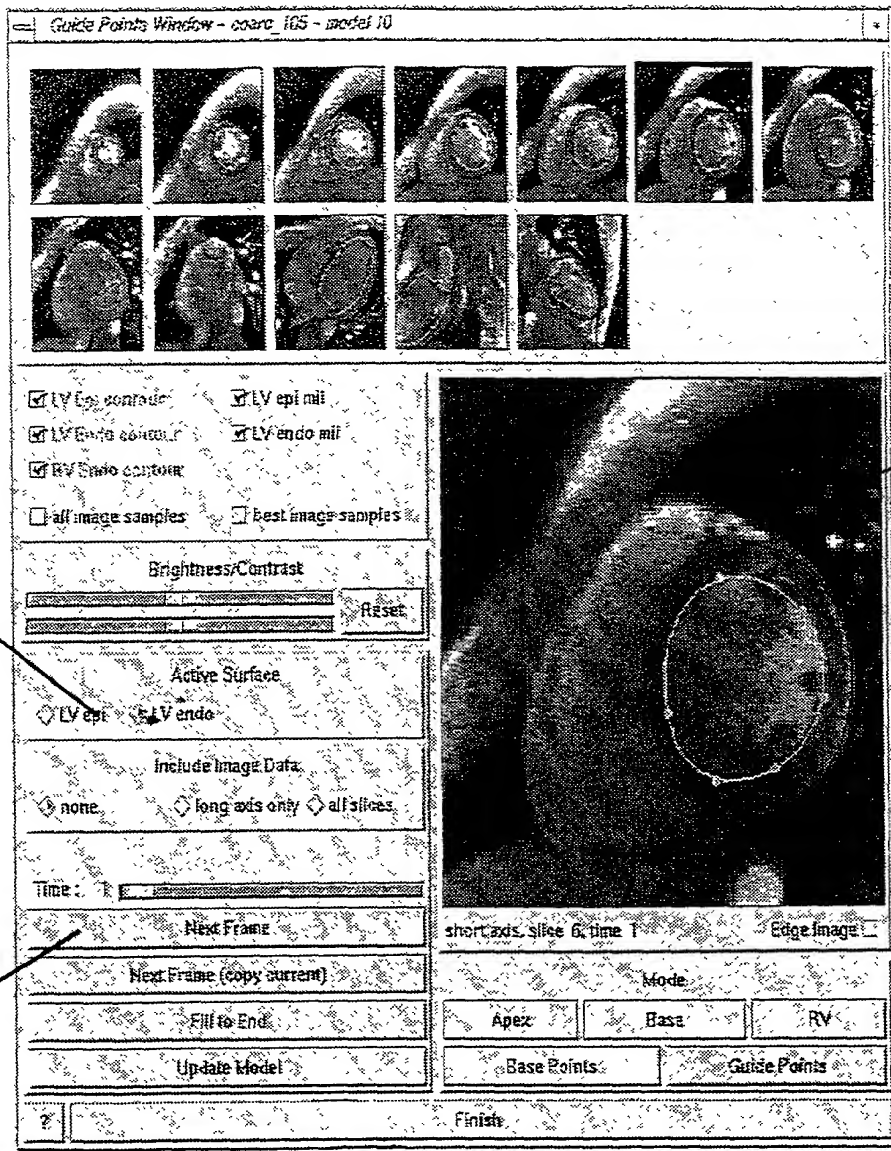
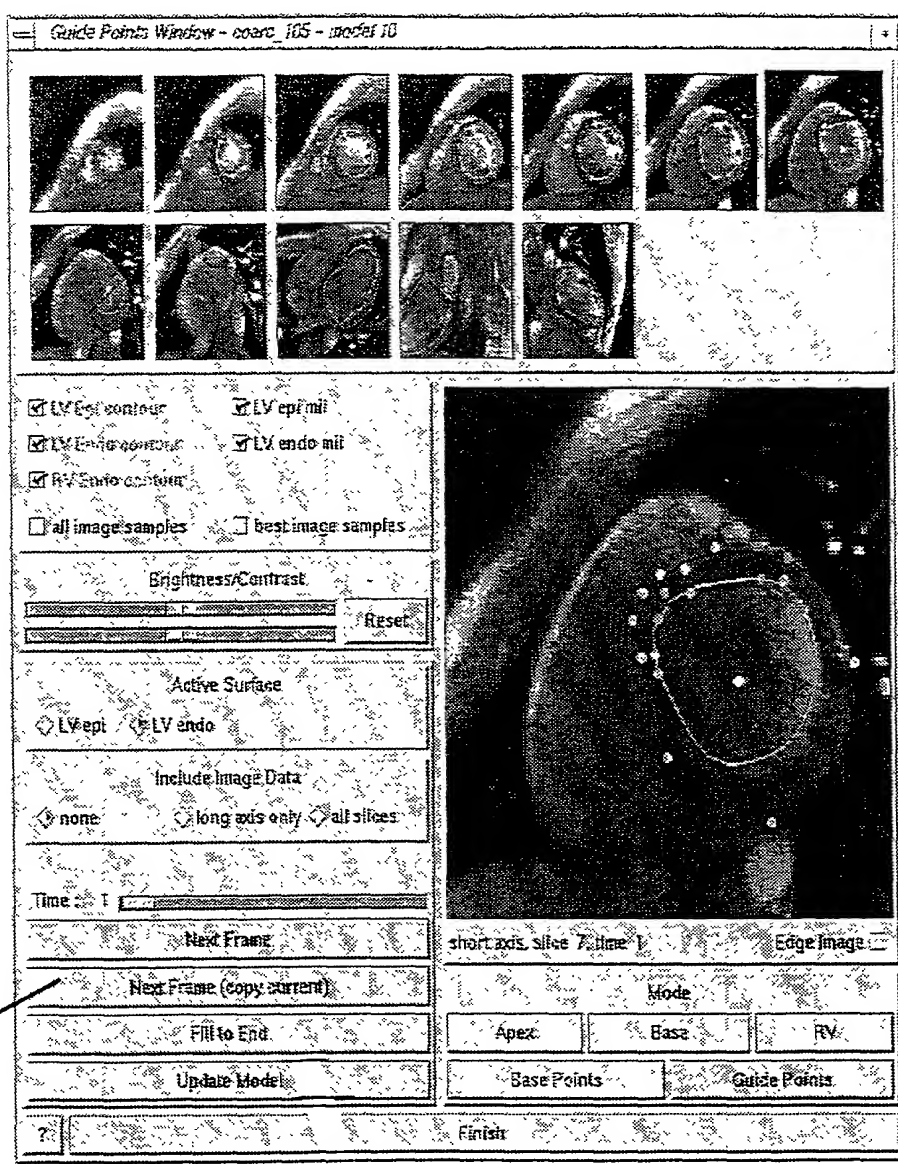


FIGURE 8

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FIGURE 9

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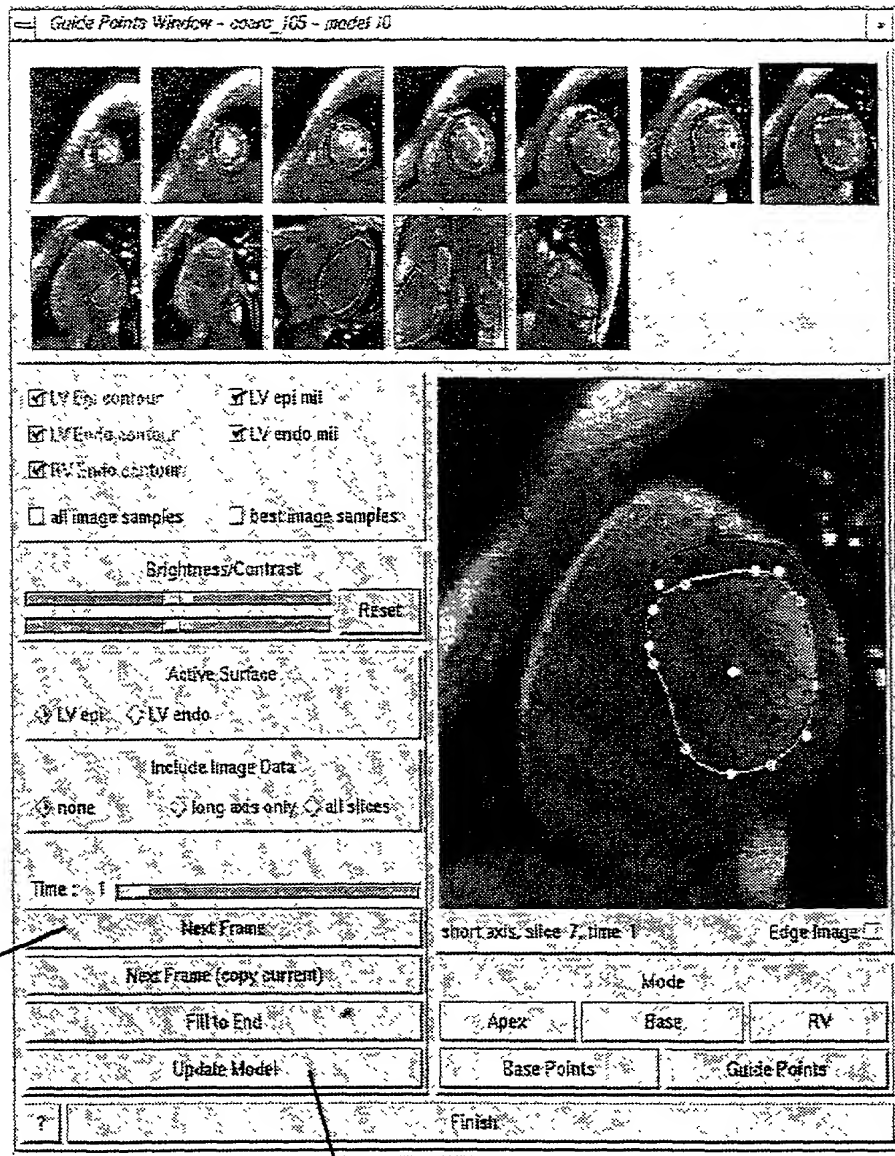
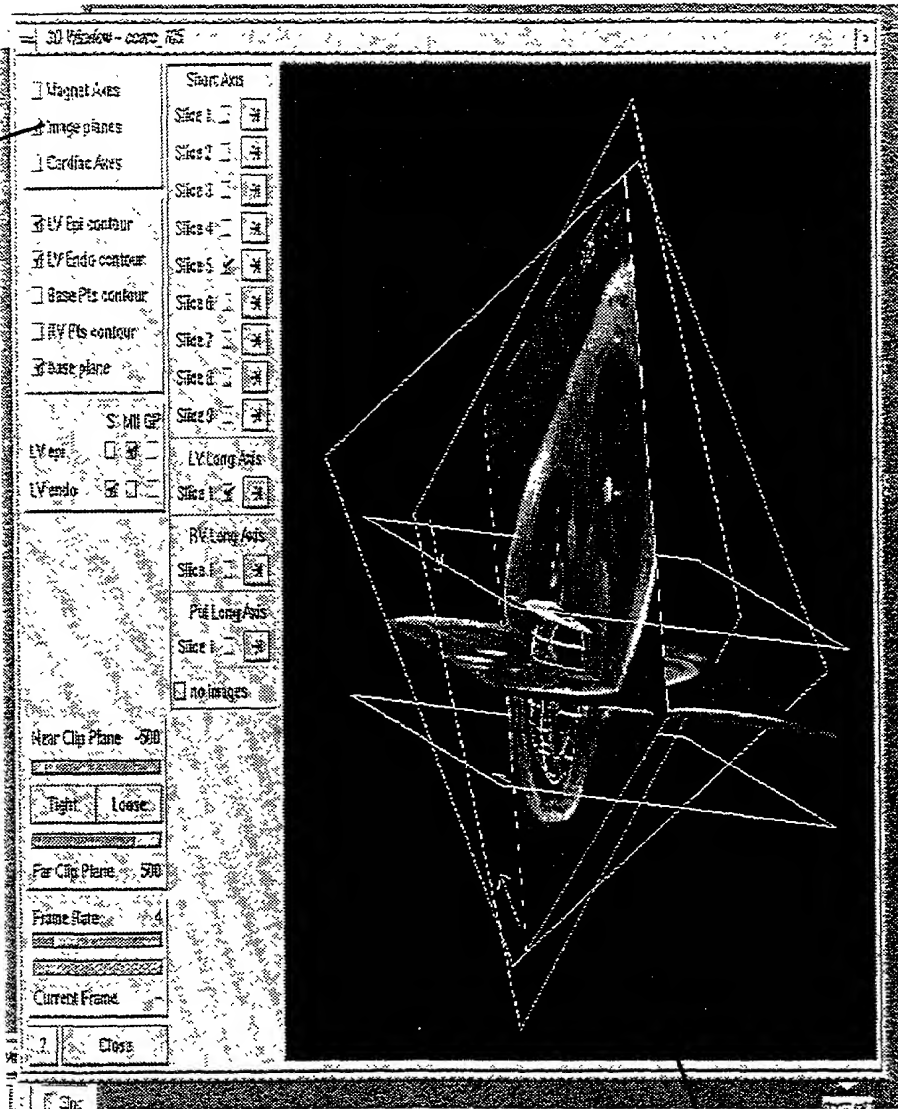


FIGURE 10

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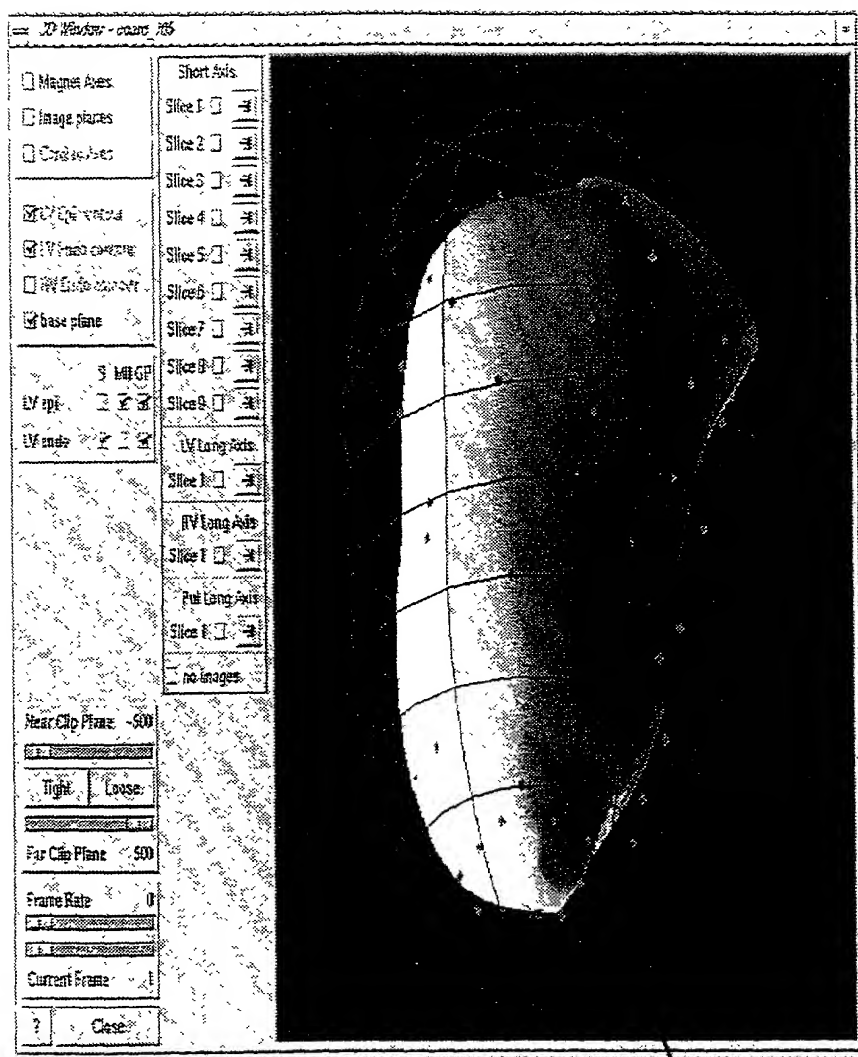


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FIGURE 11



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FIGURE 12





FIGURE 13

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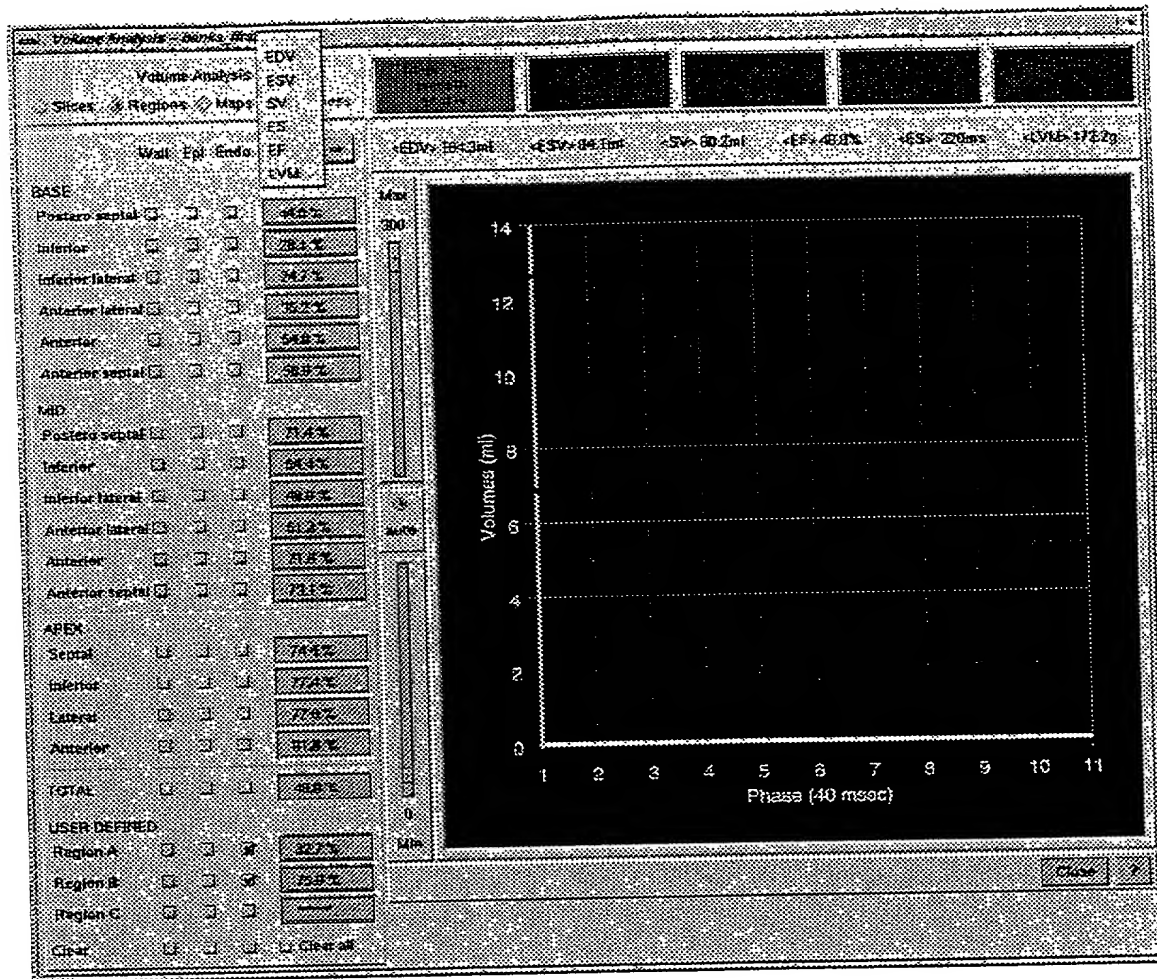


FIGURE 14

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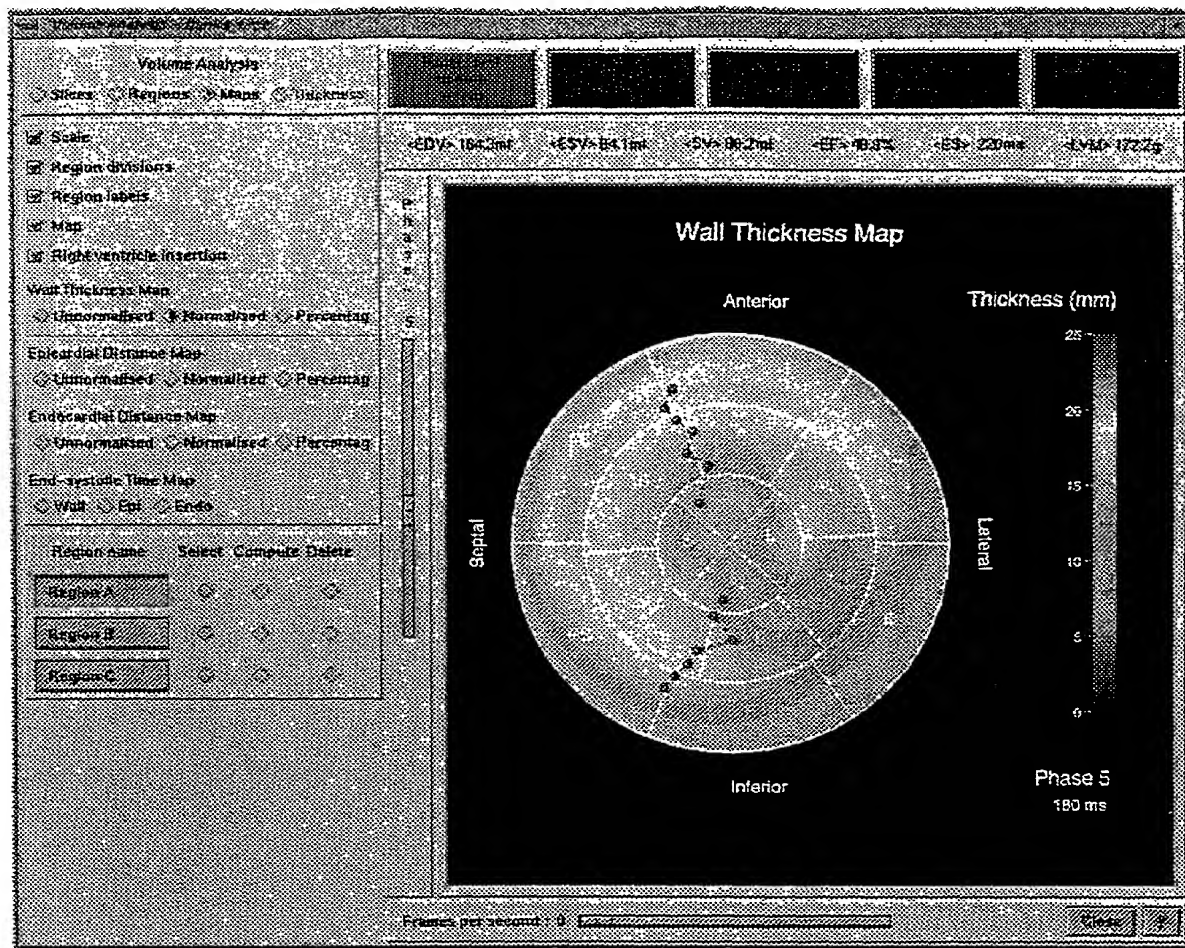


FIGURE 15

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▲  
RDNE

FROM NIXON VANDERHYE PC

(PRI) 12 15 00 15:15/ST. 15:13/NO. 4860565192 P 5

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28645 GWW/eww

Nixon &amp; Vanderhye P.C. (10/99)

(Domestic Non-Assigned/Foreign) Page 1

**RULE 63 (37 C.F.R. 1.63)**  
**INVENTORS DECLARATION FOR PATENT APPLICATION**  
**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

As a below named inventor, I hereby declare that my residence, mailing address and citizenship are as stated below next to my name, and I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**METHOD AND SYSTEM FOR MEASURING CHARACTERISTICS OF AN ORGAN**

the specification of which (check applicable box(es)):

☐ is attached hereto  
☐ was filed on \_\_\_\_\_ as U.S. Application Serial No. \_\_\_\_\_ (Att. Dkt. No. 3852-33)  
☒ was filed as PCT International application No. PCT/NZ00/00063 on 26 April 2000  
 and (if applicable to U.S. or PCT application) was amended on \_\_\_\_\_

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose to the Patent Office all information known to me to be material to patentability as defined in 37 C.F.R. 1.56. I hereby claim foreign priority benefits under 35 U.S.C. 119/365 of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed or, if no priority is claimed, before the filing date of this application:

Priority Foreign Application(s)	Country	Day/Month/Year Filed
Application Number 335321	New Zealand	21 April 1999

I hereby claim the benefit under 35 U.S.C. §119(a) of any United States provisional application(s) listed below.

Application Number	Date/Month/Year Filed

I hereby claim the benefit under 35 U.S.C. 120/365 of all prior United States and PCT international applications listed above or below:

Prior U.S./PCT Application(s)	Day/Month/Year Filed	Status: patented pending, abandoned
Application Serial No. PCT/NZ00/00063	26 April 2000	

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon. And on behalf of the owner(s) hereof, I hereby appoint NIXON & VANDERHYE P.C., 1100 North Glebe Rd., 8<sup>th</sup> Floor, Arlington, VA 22201-4714, telephone number (703) 816-4000 (to whom all communications are to be directed), and the following attorneys thereof (of the same address) individually and collectively owner's/owners' attorneys to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith and with the resulting patent: Arthur R. Crawford, 25327; Larry S. Nixon, 28640; Robert A. Vanderhye, 27078; James T. Hosmer, 30184; Robert W. Faris, 31362; Richard G. Beebe, 22770; Mark E. Nusbaum, 32348; Michael J. Keenan, 32108; Bryan H. Davidson, 30251; Stanley C. Spooner, 27393; Leonard C. Mitchard, 29009; Duane M. Byers, 33363; Jeffry H. Nelson, 30481; John R. Lastova, 33149; H. Warren Burnam, Jr., 28368; Thomas E. Byrne, 32205; Mary J. Wilson, 32855; J. Scott Davidson, 33489; Alan M. Kagan, 36178; Robert A. Moran, 29834; B. J. Sadoff, 36663; James D. Berquist, 34778; Updeep S. Gill, 37334; Michael J. Shea, 34725; Donald L. Jackson, 41080; Michelle N. Lester, 32331; Frank P. Presta, 19828; Joseph S. Presta, 35329; Joseph A. Rhca, 37515; Raymond Y. Mah, 41426. I also authorize Nixon & Vanderhye to delete any attorney names/numbers no longer with the firm and to act and rely solely on instructions directly communicated from the person, assignee, attorney, firm, or other organization sending instructions to Nixon & Vanderhye on behalf of the owner(s).

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☐ See attached sheet(s) for additional inventor(s) information!!

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